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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,407	12/08/2006	Takumi Teratani	701053	2167

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EXAMINER
NGUYEN, QUANG

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
06/09/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	10/591,407	TERATANI ET AL.
	Examiner	Art Unit
	QUANG NGUYEN	1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/29/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 3/29/2011 was entered.

Claims 8-12 are pending in the present application; and they are examined on the merits herein.

Response to Amendment

The Declarations under 37 CFR 1.132 filed 3/29/2011 and 11/16/2009 are sufficient to overcome the rejections of claims 8-13 based at least upon Loring, J. (WO 99/27076; IDS) in view of Price et al. (WO 98/30679; IDS) and Takahama et al. (Oncogene 16:3189-3196, 1998; IDS) under 35 U.S.C. 103(a).

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***This is a new ground of rejection.***

Claim 12 recites the limitation **"wherein a rat leukemia inhibitory factor (rLIF)-free culture medium is used in step (B)".** The broad claim encompasses **the use of non-rat LIF (e.g., mouse or human LIF) containing culture medium in dissociating**

the inner cell mass (step B) formed in a rat blastocyst that has been cultured in a LIF-free culture medium (step A) in a method for producing a rat embryonic stem cell and in which method a rLIF-containing culture medium is used in steps C-E. There is **no written support** in the as-filed specification for this embodiment in the above broad limitation. While originally filed specification teaches **the use of culture medium without rat LIF in the steps for the formation and separation of inner cell masses from blastocysts; or in the steps after the formation of inner cell masses (including the culture and passage of established rat ES cells) an rLIF-containing culture medium is used** (see at least page 17, line 29 continues to line 4 of page 18; and original claims 8 and 12); the specification does not teach or suggest using any non-rat LIF (rLIF-free) culture medium in the step of dissociating inner cell masses formed from a rat blastocyst that has been cultured in a LIF-free culture medium. It is noted that in the amendment filed on 8/24/2010 (page 4, second paragraph), Applicants failed to cite the specific page number and/or line number that have an alleged written support for claim 12 as amended.

Therefore, given the lack of guidance provided by the originally filed specification as discussed above, it would appear that **Applicants did not specifically contemplate or have possession of the instant broadly claimed invention at the time the application was filed**.

Enablement

Claims 8-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method of producing a rat embryonic stem cell, which method consists essentially of the following steps (A)-(E) performed using a culture medium with 2% or less serum concentration:

(A) culturing a rat blastocyst in a leukemia inhibitory factor (LIF)-free culture medium to form an inner cell mass in the blastocyst,

(B) dissociating the inner cell mass, wherein the dissociated inner cell mass is in a cell aggregate state,

(C) culturing primary embryonic stem cells resulting from a culture of the dissociated inner cell mass until the primary embryonic stem cells can be passaged,

(D) dissociating the primary embryonic stem cells, which can be passaged, wherein the dissociated primary embryonic stem cells are in a cell aggregate state, and

(E) culturing the dissociated primary embryonic stem cells to establish an embryonic stem cell,

wherein a rat leukemia inhibitory factor (rLIF)-containing culture medium is used in steps (C)-(E); and **culturing steps (A), (C) and (E) are performed on a mitomycin C-treated mouse embryonic fibroblast (feeder cell)-coated dish**;

does not reasonably provide enablement for a method of producing a rat embryonic stem cell as claimed broadly. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the invention commensurate in scope with these claims. ***This is a new ground of rejection.***

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

The instant specification is not enabled for a method of producing a rat embryonic stem cell as broadly claimed for the reasons discussed below.

1. *The breadth of the claims*

The claims are directed to a method of producing a rat embryonic stem cell which consists essentially of the steps (A)-(E) performed using a culture medium with 2% or less serum concentrations as recited in independent claim 8, **encompassing a method in which the culturing steps (A), (C) and (E) can be carried out under any conditions**, not necessarily limiting culturing a rat blastocyst in a LIF-free culture medium to form an inner cell mass in the blastocyst on a mitomycin C-treated mouse embryonic fibroblast (feeder cell)-coated dish; and/or culturing rat embryonic stem cells at steps (C) and/or (E) in a rLIF-containing culture medium on a mitomycin C-treated mouse embryonic fibroblast (feeder cell)-coated dish.

2. The state and the unpredictability of the prior art

At about the effective fling date of the present application (3/4/2004), the establishment of a true rat ES has proved difficult as evidenced at least by the teachings of Brenin et al (Developmental Biology 185:124-125, 1997; IDS); Vassilieva et al (Developmental Cell Research 258:361-373, 2000; IDS); Loring, J. (Methods in Molecular Medicine 32:240-270, 1999); Buehr et al (Biology of reproduction 68:222-229, 2003; IDS); Ueda et al (PLos One, Volume 3, Issue 7, e2800, 2008) and Buehr et al (Cell 135:1287-1298, 2008); let alone a method for producing a rat embryonic stem cell consisting essentially of the recited steps (A)-(E) performed using a culture medium with 2% or less serum concentration as claimed.

3. The amount of direction or guidance provided

Apart from disclosing the establishment of a rat embryonic stem cell in a method in which **a rat blastocyst is cultured in a LIF-free culture medium to form an inner cell mass in the blastocyst (step A) on a mitomycin C-treated mouse embryonic fibroblast (feeder cell)-coated dish**; as well as **culturing primary rat embryonic stem cells (step C) and dissociated primary rat embryonic stem cells (step E) on a mitomycin C-treated mouse embryonic fibroblast (feeder cell)-coated dish in a rLIF-containing medium**, the instant specification fails to provide sufficient guidance for a skilled artisan on how to establish a rat embryonic stem cell **in which steps A, B and C were performed under any other conditions**; especially steps A-E were required to carry out using a culture medium with 2% or less serum concentration; and the unexpected efficiency of forming rat inner cell masses in step A in a LIF-free culture medium (see 1.132 Declaration filed on 11/16/2009). The instant specification states

explicitly "**A key to the successful establishment of rat ES cells is the setting of culture conditions for the production of ES cells**. While the conventional attempts have been made based on the establishment of and culture conditions for mouse ES cells, rat ES cells have not been established as yet. From these backgrounds, it is considered that **ingenuity in the culture conditions is essential for the production of rat ES cells**" (page 3, lines 24-31). In both 1.132 Declarations filed on 11/15/2009 and 3/29/2011, rat blastocysts and rat embryonic stem cells were also cultured on a mitomycin C-treated mouse embryonic fibroblast (feeder cell)-coated dish for the establishment of a rat ES cell of the present invention. Since the prior art at the filing date of the present application failed to provide any guidance on these issues, particularly it has been known to be difficult to establish a true rat ES as discussed above, it is incumbent upon the present application to do so.

Accordingly, due to the lack of sufficient guidance provided by the specification regarding to the issues set forth above, the unpredictability of the physiological art for establishing a rat embryonic stem cell, and the breadth of the claims, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/QUANG NGUYEN/

Primary Examiner, Art Unit 1633